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PPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
08/444,790 O5/19/1995 V		MANFRED BROCKHAUS	9189 5612	
37500 75	90 04/03/2006		EXAM	INER
AMGEN INC.		6	HOWARD, Z	ACHARY C
LAW DEPART 1201 AMGEN		REGULTED	ART UNIT	PAPER NUMBER
SEATTLE, WA	98119	APR & b Loud	1646	
		AMGEN LAW DEPARTMENT	DATE MAILED: 04/03/2006	5 .

Docketed: 7-3-06

RECEIVED MANUSCREE GERSTEIN

Please find below and/or attached an Office communication concerning this application or proceeding.

Docketed: BREACH TO CA Review: SUND 7.3.656 Due Date: MAO 10.3.66 By: VAF

PTO-90C (Rev. 10/03)

	Application No.	Applicant(s)	
	08/444,790	BROCKHAUS ET	AL.
Office Action Summary	Examiner	Art Unit	
	Zachary C. Howard	1646	
- The MAILING DATE of this communication	n appears on the cover sheet wit	h the correspondence ad	dress
eriod for Reply			
A SHORTENED STATUTORY PERIOD FOR R WHICHEVER IS LONGER, FROM THE MALIN Extendence of time may be available under the provision of 70 of the SV (8) (MVITHS from the making date of this communical. If NO period for repty is specified above, the maximum statutory. Failure to repty with the set or contended period for repty will by Any reply received by the Office later than three months after the earned period for tempty will be available to 80 of 70 cm. 170 cm.	NG DATE OF THIS COMMUNIC CFR 1.136(a). In no event, however, may a re on. period will apply end will expire SIX (0) MONT statute, cause the application to become ABA	ATION. ply be timely filed "HS from the mailing date of this or ANDONED (35 U.S.C. § 133).	,
atus			
1) Responsive to communication(s) filed on	05 October 2005.		
·= ·	This action is non-final.		
3) Since this application is in condition for al	llowance except for formal matte	ers, prosecution as to the	merits is
closed in accordance with the practice un	nder Ex parte Quayle, 1935 C.D.	11, 453 O.G. 213.	
isposition of Claims			
4) Claim(s) 62,66,67,102-107,110-114 and	119-138 is/are pending in the ar	nlication	
4a) Of the above claim(s) is/are wit			
5) Claim(s) is/are allowed.			
6) Claim(s) 62.66,67,102-107,110-114 and	119-138 is/are rejected.		
7) Claim(s) is/are objected to.			
8) Claim(s) are subject to restriction a	and/or election requirement.		
oplication Papers			
9) The specification is objected to by the Exa	eminer.		
10) The drawing(s) filed on 19 May 1995 is/an	e: a)⊠ accepted or b)□ objec	ted to by the Examiner.	
Applicant may not request that any objection t	to the drawing(s) be held in abeyan	ce. See 37 CFR 1.85(a).	
Replacement drawing sheet(s) including the c			
11) The oath or declaration is objected to by the	he Examiner. Note the attached	Office Action or form PT	TO-152.
riority under 35 U.S.C. § 119			
12) Acknowledgment is made of a claim for fo a) All b) Some * c) None of;	reign priority under 35 U.S.C. §	119(a)-(d) or (f).	
1.⊠ Certified copies of the priority docu	ments have been received.		
	ments have been received in A	plication No.	
3. Copies of the certified copies of the	priority documents have been	received in this National	Stage

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/S8/08)

Paper No(s)/Mail Date 3/28/05, 2/21/05.

4) 🔲	Interview Summary (PTG	0-41
	Paper No(s)/Mail Date.	

5) Notice of Informal Patent Application (PTO-152)
6) Other:

U.S. Petent and Trademark Office PTOL-326 (Rev. 7-05)

AMGEN

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DETAILED ACTION

The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Zachary C. Howard, Art Unit 1646, Technology 1600.

Status of Application, Amendments and/or Claims

The amendment of 10/5/05 and the supplemental amendments of 12/14/05 and 2/21/06 have been entered in full. In the 10/5/05 amendment, claims 62, 66, 102, 104-110 and 112-114 are amended. Claims 63-65, 68-101, 108, 109 and 115-118 are canceled. New claims 119-138 are added. In the 12/14/05 amendment, claims 102-105, 112, 113, 123, 124, 132 and 133 are amended, and new claim 138 is added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 62, 66, 67, 102-107, 110-114 and 119-138 are under consideration in the instant application.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 3/28/2005 and 2/21/2006 have been considered by the examiner.

The information disclosure statement filed 12/20/05 fails to comply with 37 CFR 1.98(a)(5), which requires the following: "a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered." The IDS filed 12/20/05 lacks a heading clearly indicating that the list is an information disclosure statement. As stated in MPEP 609 [R-3]: "Information submitted to the Office that does not comply with the requirements of 37 CFR 1.97 and 37 CFR 1.98 will not be considered by the Office but will be placed in the application file."

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Priority

- (1) In view of the papers filed 2/21/2006, European Patent Application No. 99100703.0, filed August 31, 1990, is added to the foreign priority claim of the present application (under 35 USC 119 (a-d)). Applicants have submitted a Request to Correct the Filing Receipt. The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the priority as corrected.
- (2) It is noted that the Foreign Applications SWITZERLAND 3319/89 09/12/1989 and SWITZERLAND 746/90 03/08/1990, to which the present application claims priority, do not disclose the sequence of SEQ ID NO: 4. It is further noted that the Foreign Application SWITZERLAND 1347/90 4/20/1990, to which the present application claims priority, does not disclose the exact sequence of SEQ ID NO: 4. Rather, 1347/90 discloses an amino acid sequence in Figure 4 that differs from SEQ ID NO: 4 at residue 3. 1347/90 has a 'Ser' at residue 3 in Figure 4 while instant SEQ ID NO: 4 has a 'Thr' at residue 3. In the papers filed 1/18/2005, Applicants stated, "Applicants note that SEQ ID NO: 3 and 4 are identical to Figure 4 except they also include the sequence correction noted at page 35, lines 32-36 of Example 8 (amino acid at position 3 is Thr instead of Ser as it is encoded by "ACC" not "TCC")" (pg 14). However, Example 8 of 1347/90 does not appear to disclose this correction. Therefore, with regard to sequences comprising the entirety of SEQ ID NO: 4, the instant application does not merit priority to the filing date of 1347/90.

Furthermore, 1347/90, while disclosing a partial sequence of the extracellular region of TNF2R (Figure 4), does not appear to disclose fusion proteins comprising TNF2R and "all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region" (as set forth in the claims). Support for this limitation is set forth in the instant application at pg 11, lines 1-10, as noted by Applicants in the 1/18/05 response when the limitation was added to the claims. However, the 1347/90 application does not appear to disclose this information.

It is further noted that Foreign Application EPO 99100703.0 8/31/1990, to which the present application also claims priority, does appear to disclose SEQ ID NO; 4 (in

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the form of Figure 4 and the amino acid change at residue 3 noted in Example 8), and fusions of said sequence with the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region. Therefore, with regard to fusion proteins comprising the sequence of SEQ ID NO: 4 and "all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region", the instant application is entitled priority to 8/31/1990, which is the filling date of EPO 99100703.0.

Specification

The disclosure is objected to because of the following informalities:

- (1) An <u>updated</u> priority statement of the instant application's parent provisional and nonprovisional applications should be included in the first sentence of the specification or application data sheet. This priority statement was last updated in the preliminary amendment of 5/19/1995. Specifically, this statement should be amended to indicate that application 08/095,640 has been issued as U.S. Patent 5,610,279 (7/21/1993) and also that application 07/580,013 has been abandoned.
- (2) The title of the invention ("HUMAN TNF RECEPTOR") is not descriptive because the claims are all directed to a human TNFR immunoglobulin fusion protein. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "HUMAN TNF RECEPTOR IMMUNOGLOBULIN FUSION PROTEIN."

Appropriate correction is required.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (4/5/2005).

All rejections of claims 63, 65, 68-71, 75-77, 100, 101, 108, 109 and 115-118 are withdrawn in view of Applicants' cancellation of the claims.

The rejection at pg 2-4 of claims 62, 66, 67, 102-107, 110-114 and 119-137 under the judicially created doctrine of obviousness type double patenting as being

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obvious over claims 1 and 4 of U.S. Patent No. 5,610,279 is *withdrawn* in view of Applicants' amendments to the claims.

The rejection at pg 5 of claims 62, 66, 67, 102-107, 110-114 and 119-137 under 35 U.S.C § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicants' arguments.

Please see new claim rejections, below.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

Claims 123, 124, 132 and 133 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel biological materials. Specifically, new claims 123, 124, 132 and 133 claim proteins comprising the constant region of the human immunoglobulin heavy chain encoded by the plasmids pCD4Hγ1 or pCD4Hγ4. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 U.S.C § 112 may be satisfied by a deposit of the biological materials. It is noted that the specification indicates (pg 17, lines 25-31) that pCD4Hγ1 and pCD4Hγ4 have been deposited at the Deutschen Sammlung von Mikroorganism (DSM) in Braunschweig, FRG as accession numbers DSM5314 and DSM5523. Applicants have deposited the biological materials (p. 17 of the specification). However, there is no indication in the specification as to public availability.

If a deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicant(s) or person associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the

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Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R.§1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, should be submitted stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

- (a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;
- (b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent:
- (c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;
- (d) a viability statement in accordance with the provisions of 37 C.F.R.§1.807; and
- (e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the Identifying information set forth in 37 C.F.R.§1.809(d) should be added to the specification. See 37 C.F.R.§§ 1.803-1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 62, 66, 67, 102-107, 110-114 and 119-138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35

U.S.C. § 112, paragraph 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicants are claiming and what Applicants have possession of.

The claims are genus claims because the claims are directed to variant polypeptides that specifically bind human TNF. The polypeptides comprise two parts: (a) a soluble fragment of a receptor; and (b) "all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region". In claim 62, part (a) encompasses a protein comprising any soluble fragment of receptor comprising a fragment of SEQ ID NO: 4. The sequence of SEQ ID NO: 4 consists of 392 amino acids (also shown in Figure 4) and represents a partial sequence of the full-length human tumor necrosis factor type II receptor (TNF-IIR or TNF2R; also known variously as p75 or p80 based on the molecular weight on a SDS-polyacrylamide gel). The full-length mature human TNF2R is 439 amino acids, with the extracellular portion consisting of amino acids 1-235 (see pg 233 and Figure 1 of Dembic et al, 1990. Cytokine, 2(4): 231-7). Instant SEQ ID NO: 4 represents only a portion of the full-length TNF2R sequence; specifically, instant SEQ ID NO: 4 is missing amino acids 1-48 found in the full-length mature TNF2R. Therefore, instant SEQ ID NO: 4 is missing the first 48 amino acids of the extracellular domain (approximately 20% of the extracellular domain). Applicants further disclose a sequence consisting of 17 of the 18 N-terminal amino acids of the full-length TNFR2 (see pg 33; SEQ ID NO: 10). Together, SEQ ID NO: 4 and 10 consist of only a portion of the TNF2R extracellular domain (residues 1-7, 9-18 and 49-235).

The relevant art teaches that the extracellular domain of human TNF2R is the portion of the protein that binds human TNF. Chan et al teaches, "The deletion of PLAD [protein-ligand assembly domain] from either p60 or p80 completely abrogated ligand binding (Table 1 and Fig. 1E)" (pg 2351 of Chan et al. 2000, Science, 288: 2351-2354). Chan teaches that the PLAD is amino acids 10-54 of the receptor (pg 2351). Furthermore, specific single or double mutations in this region in the TNFRI receptor

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"eliminated TNF-α binding" (pg 2351). Chan concludes "the PLAD is physically distinct from the ligand contact domain but nonetheless essential for efficient TNF-α binding and receptor function." In view of the teachings of Chan, the truncated receptor of SEQ ID NO: 4 taught by Applicants would not have the ability to bind TNF, as required by the claims.

The claimed protein comprises <u>any</u> soluble fragment of TNFR2 that comprises <u>any</u> fragment of SEQ ID NO: 4. Therefore, this fragment can be as long as the entire extracellular domain (comprising the entirety of SEQ ID NO: 4), or it can be as small as one amino acid from SEQ ID NO: 4. However, Applicants do not teach any amino acid sequence that can actually bind TNF. Applicants do not disclose any teachings demonstrating that SEQ ID NO: 4 (missing 48 amino acids of the extracellular domain of TNFR2) can bind to TNF. Therefore, the specification has not described a single example of a protein in the claimed genus that can actually bind human TNF.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics. i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of any member of the genus of claimed polypeptides. Neither the specification nor the claims describe a TNF2R protein sequence that can bind to TNF-α. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

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Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed," (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that The or shell invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPO2d 1481 at 1483. In Fiddes, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the instant claims do not meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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Claims 62, 66, 67, 102-107, 110-114, 119-122, 125-131 and 134-138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dembic et al (Cytokine, Vol. 2, No. 4 (July) 1990: 231-237) in view of Capon et al, U.S. Patent No. 5,116,964, published 26 May 1992 and filed 22 November 1989.

As noted above, in the section titled "Priority", 31 August 1990 is the earliest date for which the claimed protein comprising SEQ ID NO: 4 and Ig domains is entitled priority.

Claims 62, 66, 67, 102-107, 110-114, 119-122, 125-131, 134-136 and 138 each encompass a genus of variant polypeptides. While the scope of each genus varies, each encompasses the following polypeptide: a purified protein, recombinantly produced in CHO cells, that specifically binds human TNF and comprises parts (a) and (b).

Part (a) of each claim encompasses a soluble fragment of a receptor, wherein the receptor has three characteristics: (i) binds TNF; (ii) 75 kDa molecular weight; and (iii) "comprises a fragment of the amino acid sequence set forth in SEQ ID NO: 4" or "is encoded by a nucleic acid sequence comprising a fragment ... of SEQ ID NO: 3" (SEQ ID NO: 3 encodes SEQ ID NO: 4). Characteristic (iii) encompasses any sequence comprising any fragment of SEQ ID NO: 4; that is, comprising any shorter sequence found within the sequence of SEQ ID NO: 4. In other words, any longer sequence that includes a shorter sequence found within SEQ ID NO: 4 meets the limitation of a fragment that comprises a "fragment of the amino acid sequence set forth in SEQ ID NO: 4" or "encoded by a nucleic acid sequence comprising a fragment ... of SEQ ID NO: 3" (because SEQ ID NO: 4 is encoded by SEQ ID NO: 3). The narrowest claims also include the limitation that the soluble fragment comprises the following peptides: LCAP, VFCT, and peptide LPAQVAFXPYAPEPGSTC (wherein X is any amino acid as taught on pg 33 of the specification); however, each of the claims encompasses a protein including these three peptides.

Part (b) of each claim encompasses "all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant

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region". The narrowest claims limit immunoglobulin heavy chain to human IgG1; however, all of the claims encompass this limitation.

Dembic teaches the full-length amino acid sequence of the 75kDa Tumor Necrosis Factor receptor (see pg 232 and Figure 1). This receptor meets the three characteristics of the receptor of claim 62: (i) it binds TNF; (ii) 75kDa; and (iii) comprises a numerous fragments of the sequence set forth in SEQ ID NO: 4. Furthermore, as shown in Figure 1, the sequence taught by Dembic comprises the following peptides within the extracellular domain: LCAP (residues 114-117), VFCT (residues 43-47) and peptide LPAQVAFXPYAPEPGSTC (residues 1-18; this peptide meets the sequence LPAQVAFXPYAPEPGSTC). Dembic further teaches the extracellular domain of this receptor forms a soluble fragment that binds TNF (see pg 234, column 1).

Dembic does not teach a fusion of the extracellular domain of the 75 kDa TNF receptor with any portion of the constant region of a human immunoglobulin heavy chain.

Capon teaches (Example 4, starting at column 40) a fusion of truncated murine lymphocyte homing receptor (MHLR) to the Fc region of human IgG1 ("These truncated proteins are all joined to a human heavy chain y 1 region just upstream of the hinge domain (H) such that these chimeras contains the two cysteine residues of the hinge responsible for dimerization as well as the CH2 and CH3 constant regions." The Fc region consists of the CH2 and CH3 domains of the constant region but does not include the CH1 domain. Capon further teaches that the hybrid immunoglobulins can be used for affinity purification of ligands (col 22, lines 5-6). Capon further teaches Capon further teaches recombinant production of hybrid immunoglobulins in cell culture (col 26, lines 24-26). Capon further teaches that CHO cells are suitable eukaryotic cells for production of hybrid immunoglobulins (col 29, line 37). Capon further teaches purification of the hybrid immunoglobulin from cell cultures following expression in host cells (col 30, line 26-27). Capon further teaches placement of the purified hybrid immunoglobulin in "sterile, isotonic formulations" that are "preferably liquid" and "ordinarily a physiologic salt solution" (col 31, lines 4-8). Such solutions meet the definition of a "pharmaceutically acceptable carrier material" (as in claim 114).

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It would be obvious to the person of ordinary skill in the art at the time the invention was made to fuse the extracellular portion of the TNF receptor sequence taught by Dernbic to the Fc region taught by Capon, and to recombinantly produce the protein in CHO cells and purify the protein produced as taught by Capon. The person of ordinary skill in the art would be motivated to do so in order to produce and purify the TNF receptor-Ig fusion for use in affinity purification of the TNF ligand. The person of ordinary skill in the art would have expected success because Capon teaches that Ig fusions can be made with a wide variety of proteins, and teaches all of the techniques for recombinant production of hybrid immunoglobulins in CHO cells and purification of the produced protein.

With respect to claims 114 and 137, the recitation of "a pharmaceutical composition" in the preamble of the claim is interpreted as an intended use and bears no accorded patentable weight. Therefore, the claims encompass any composition comprising a recombinant protein of claims 62, 66, 107, 134 or 135 (claim 114) or claim 105 (claim 137) and a pharmaceutically acceptable carrier material. As described above, Capon teaches compositions comprising a hybrid immunoglobulin in a pharmaceutically acceptable carrier material. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to further include the hybrid TNF receptor-immunoglobulin in a pharmaceutically acceptable carrier material. The person of ordinary skill in the art would be motivated to do so in order to resuspend the hybrid immunoglobulin for use following purification. The person of ordinary skill in the art would have expected success because Capon teaches the necessary procedures for purification and resuspension of the hybrid immunoglobulin.

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Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

zch

LORRAINE SPECTOR PRIMARY EXAMINER



PTO/SB/08a/b (08-03 Approved for use through 07/31/2006, OMB 0851-0031 atons and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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Şut	stitute for form 1449A/B/PT	TO		Complete if Known			
l				Application Number	08/444,790-Conf. #5612		
	NFORMATION			Filing Date	May 19, 1995		
S	STATEMENT BY APPLICANT		APPLICANT	First Named Inventor	Manfred Brockhaus		
				Art Unit	1646		
	(Use as many sheets as necessary)			Examiner Name	J. Murphy Zach Howard		
Sheet	1	of	8	Altomey Docket Number	01017/40451B		

	_		U.S. FP	TENT DOCUMENTS	
Examiner Initials	Cite No.1	Document Number Number-Kind Code ² (# Known)	Publication Date MM-DD-YYYY	Name of Patentos or Applicant of Cited Document	Pages, Columns, Lines, When Relevent Passages or Releva Figures Appear
-2M	A11	08/478,995	N/A	Lauffler, Leander et al.	
14.	A12	2003/064480	04-03-2003	Lauffler, Leander et al.	
	A13	4,593,002	01-11-1982	Dulbecco	
	A14	4,675,285	09-19-1984	Clark et al.	
	A15	4,729,326	03-08-1988	Richter	
	A16	4,769,326	09-06-1988	Rutler	
	A17	4,894,439	01-16-1990	Dorin et al.	1
	A18	4,912,044	03-27-1990	Jacob et al.	1
	A19	4,935,233	06-19-1990	Bell et al.	
	A20	4,963,354	10-06-1990	Shepard et al.	
	A21	4,965,271	10-23-1990	Mandell et al.	
	A22	5,055,447		Palladino et al.	+ +
	A23	5,073,627		Curtis et al.	+ - /-
	A24	5,075,222		Hannum et al.	
	A25	5,098,702		Zimmerman et al.	1-1-
	A26	5.098.833	03-24-1992	Lacky at al	
7-1	A27	5,118,500	06-02-1992	Hanel et al	I - /
	A28	5,136,021		Dembinski et al.	
	A29	5,155,027		Sledziewski et al.	1 /
	A30	5.211.395	06-29-1993		1 /
	A31	5.211.945	05-18-1993		1
	A32	5,225,538	07-06-1993	vvaliach et al.	1
	A33	5,258,498	11-02-1993	Capon et al.	-\-\-\-\-\-\-\-\-\-\-\-\-\-\-\-\-\-\-\
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				Art Unit	1646	
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S	STATEMENT BY APPLICANT		First Named Inventor	Manfred Brockhaus			
	(Use as many sheets as necessary)			Art Unit	1646		
				Examiner Name	J. Murphy Z. Howard		
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